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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,835	12/24/2001	Yunik Chang	HME/7679.012	9339

29085 7590 11/04/2003

HOWARD EISENBERG, ESQ.
2206 APPLEWOOD COURT
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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 11/04/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/033,835	CHANG ET AL.	
	Examin r .	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *25 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *24-81* is/are pending in the application.

4a) Of the above claim(s) *74-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *24-73,80 and 81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

Claims 1-23 have been canceled. Claims 24, 40, and 41 have been amended. Claims 45-81 have been added. Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Newly submitted claims 74-79 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Previously of record were methods for preparing compositions comprising MTZ, β–CD and niacin or niacinamide. Newly added method for increasing the solubility of MTZ by combining it with β–CD and niacin or niacinamide would be in the scope of examining the original composition. However, the method recited in claims 74-79 is distinct because it is drawn to the enhancement of the solubilizing effect of the β–CD, per se. This is a separate method from what has already been examined.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 74-79 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections

Claim 54 is objected to because of the following informalities: The claim recites "1/0%" where it appears that "1.0%" is intended. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

Claims 47 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 recites, "the solubility enhancing agent is niacin." However, the claim depends from claim 46 that recites, "the solubility enhancing agent is niacinamide." It is not clear if there is an error in dependency wherein the claim is meant to depend from claim 45 or if a combination of niacin and niacinamide is required. The claim is rendered vague and indefinite.

Claim 59 depends from canceled claim 1, thus rendering the claim vague and indefinite.

Claim Rejections - 35 U.S.C. § 103

Claims 24, 27-29, 31, 32, 40, 41, 43, and 44 are again rejected under 35 U.S.C. 103(a) as being obvious over KATA et al (Acta Pharm. Hung., 1984) and CHIEN et al (US 4,032,645), as set forth in the previous Office action. Newly added claims 45-58, 63, 65-68, 71-73, 80, and 81 are also rejected as being obvious over these references.

The invention is as set forth above in the previous Office action. Newly added claims 45-58 are drawn to an aqueous solution similar to that recited in canceled claims 1-23 wherein the scope is limited to the use of β–CD. Claims 63, 65-68, 71-73 are drawn to a method of increasing the solubility of MTZ by combining it with β–CD and niacin or niacinamide in aqueous fluid. Claims 80 and 81 recite a limitation to the method recited in claim 24 and a product-by-process prepared thereby, respectively.

Applicant's arguments filed September 25, 2003 have been fully considered but they are not persuasive.

Applicant first notes that neither of the references teaches all of the required components. The examiner agrees, and this was clearly stated in the previous Office action. The rejection was one of obviousness, not anticipation. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant further contends that there is no suggestion to combine the components as presently claimed. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, CHIEN clearly identifies niacin/niacinamide as solubility enhancing agents for MTZ, just as KATA identifies β–CD as such an agent for MTZ. As was discussed in the previous Office action, the motivation comes from the anticipated additive effects derived from combining these agents. It is obvious to combine ingredients which have been separately employed for a particular purpose in order to obtain the expected combination of benefits.

This rejection is based upon the well established proposition of patent law that no patentable invention resides in combining old ingredients of known characteristics where the results obtained thereby are no more than the additive effect of the ingredient.

Applicant further states that "the combination of betacyclodextrin and nicotinamide or niacin produces unexpected advantageous properties to the aqueous solubility of netronidazole" and cites Example 5 of the specification. The examiner has studied all the data disclosed in the specification and finds it unpersuasive. Example 5 refers to data set forth in Table 6. This data purports to show some synergistic effect on the solubility of MTZ. The examiner respectfully disagrees. In the stable 1.0% solution of MTZ (last entry), the solution comprises 0.5% niacin. It is noted in Table 5, 0.5% niacin/1.0% MTZ results in crystal formation 7 out of 8 samples. One of ordinary skill would surmise from the data that some amount of niacin, slightly greater than 0.5%, would solubilize 1.0% MTZ. It is further noted that 0.5% β–CD solubilizes 0.8% MTZ. Due to additive solubilizing effects, it is not surprising that an amount of niacin that alone appears to be close to being able to solubilize this amount of MTZ in combination with an amount of β–CD that is known to solubilize 0.8% MTZ will solubilize 1.0% MTZ.

With regard to the newly added claims drawn to a method of increasing the solubility of MTZ, as discussed in the previous Office action, it would have been obvious to prepare the recited solutions comprising MTZ, β–CD, and either niacin or niacinamide, because both β–CD and niacin/niacinamide were known to be solubilizing agents for MTZ. Therefore, it follows that it would also be obvious to one having ordinary skill in the art at the time the invention was made to use this combination of known solubilizing agents to increase the solubility of MTZ.

With regard to newly added claims 80 and 81, in the absence of unexpected results, it would have been obvious to use any available form of β–CD, such as crystalline. Products-by-process were discussed in the previous Office action.

Claims 26, 30, 33-39, and 42 are again rejected under 35 U.S.C. 103(a) as being obvious over KATA et al (Acta Pharm. Hung., 1984) and CHIEN et al (US 4,032,645) as applied to claims 24, 27-29, 31, 32, 40, 41, 43-58, 63, 65-68, 71-73, 80, and 81 and further in view of CZERNIELEWSKI (US 5,849,776), as set forth in the previous Office action. Newly added claims 59-62, 64, and 70 are also rejected as being obvious over these references.

The invention is as set forth in the previous Office action.

Applicant's arguments filed September 25, 2003 have been fully considered but they are not persuasive.

Applicant first notes that neither of the references teaches all of the required components. The examiner agrees, and this was clearly stated in the previous Office action. The rejection was one of obviousness, not anticipation. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references, as discussed above.

Applicant argues that the instant specification discloses evidence of unexpected results. The evidence of purported unexpected results was found to be unpersuasive, as discussed above.

With regard to claim 70, it was established that the preparation of a gel comprising these components would be obvious for its utility in the treatment of dermatological ailments. In the absence of unexpected results, it would be within the scope of the artisan to add components in an appropriate manner.

Claim 25 is rejected under 35 U.S.C. 103(a) as being obvious over KATA et al (Acta Pharm. Hung., 1984) and CHIEN et al (US 4,032,645) as applied to claims 24, 27-29, 31, 32, 40, 41, 43-58, 63, 65-68, 71-73, 80, and 81 and further in view of LOFTSSON (US 5,324,718), as set forth in the previous Office action. Newly added claim 69 is also rejected as being obvious over these references.

The invention is as set forth in the previous Office action.

Applicant's arguments filed September 25, 2003 have been fully considered but they are not persuasive.

Applicant first notes that neither of the references teaches all of the required components. The examiner agrees, and this was clearly stated in the previous Office action. The rejection was one of obviousness, not anticipation. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references, as discussed above.

Applicant further argues that the LOFTSON disclosure is limited to the combination of a cyclodextrin and a polymer. The examiner respectfully disagrees with this characterization. As was noted in the previous Office action, LOFTSON was applied to teach the addition of a pharmaceutical agent, with MTZ being specifically suggested, after the other components have been added to the water.

Applicant argues that the instant specification discloses evidence of unexpected results. The evidence of purported unexpected results was found to be unpersuasive, as discussed above.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Monday-Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
November 3, 2003

JAMES O. WILSON
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